S/N 09/606,137 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant: MICHAEL E. MOSELEY et al. Examiner: JUNG, William
Serial No.: 09/606,137 Group Art Unit: 3737
Filing Date: 28 JUNE 2000 Docket: 500.003US1
Title: IMAGING METHOD FOR VISUALIZING IMPLANTED LIVING CELLS

REPLY BRIEF

MAIL STOP: APPEAL BRIEF - PATENTS
P.O. BOX 1450
Commissioner for Patents
Alexandria, VA22313-1450

Sir:

The U.S. Patent and Trademark Office is hereby authorized to debit any costs and fees associated with this Petition to Deposit Account No. 50-1391. Applicants submit this REPLY BRIEF after receipt of the Examiner's Answer and in response to new issues raised therein. **A PERSONAL APPEARANCE IS REQUESTED AND THE FEE FOR THE PERSONAL APPEARANCE ON BEHALF OF THE SMALL ENTITY ASSIGNEE WAS ALREADY PAID ON MAY 12, 2008, AFTER WHICH THE PTO WITHDREW THE CASE FROM APPEAL. NO SECOND OR ADDITIONAL FEE IS NEEDED.**

CERTIFICATE UNDER 37 C.F.R. 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described herein, are being sent by facsimile transmission or deposited in the United States Postal Service, as first class mail, with sufficient postage, in an envelope addressed to: MAIL STOP: APPEAL BRIEF - PATENTS, P.O. BOX 1450, Commissioner for Patents, Alexandria, VA 22313-1450 on 8 APRIL 2010.

Mark A. Litman
Name

Signature

STATUS OF CLAIMS

Claims 5-7, 9, 11-26, 29 and 54-64 are all of the claims remaining in this application, all other claims having been voluntarily cancelled during prosecution of this application, Applicants reserving the rights to file continuation application son the subject matter of those cancelled claims and other subject disclosed but not claimed in this Application.

Claims 5, 6, 13, 14, 17, 18, 20, 21, 25, 26, 54, 55, 57 and 59 have been finally rejected under 35 U.S.C. 102(b) as anticipated by U.S. Patent No. 5,869,463 (Major). **All of these claims are on Appeal.**

Claims 7, 9, 11, 12, 15, 16, 19, 22, 29, 56 and 58 have been rejected under 35 U.S.C. 103(a) as unpatentable over U.S. Patent No. 5,869,463 (Major) in view of U.S. Patent No. 5,497,770 (Morcos et al.) **All of these claims are on Appeal.**

Claim 23 has been rejected under 35 U.S.C. 103(a) as unpatentable over U.S. Patent No. 5,869,463 (Major) in view of U.S. Patent No. 6,567,684 (Chenevert). **All of these claims are on Appeal.**

Claim 24 has been rejected under 35 U.S.C. 103(a) as unpatentable over U.S. Patent No. 5,869,463 (Major) in view of U.S. Patent No. 6,140,116 (Dinsmore). **All of these claims are on Appeal.**

Claims 60-64 were inadvertently dropped from claims in a first Brief on Appeal filed 27 January 2007, and in an amendment filed 26 February 2007 after withdrawal of the Final Rejection by the US Patent and Trademark Office. These claims must therefore be considered *de facto* CANCELED and are so noted in the set of claims on Appeal. Claims 60-64 are therefore NOT on Appeal and are Canceled.

Claims 5-7, 9, 11-26, 29 and 54-59, all of the pending claims in this Application are On Appeal in this Appeal.

NEW ISSUES RAISED IN THE EXAMINER'S AMENDMENT

The fundamentally new approach to the rejection is an attempt to associate nearly immaterial statements in the Major reference to imply instruction of concepts recited in the claims that are completely absent from the teachings of Major as adistinct series of process steps. To appreciate this, first the subject matter of the claims must be appreciated, and then the use of the random statements in Major to imply (yet never teach) these steps must be analyzed.

Claim 5 (Summary)

a) Cells are grown in a culture;

b) The cells are implanted;

c) After implantation, the region of implantation is viewed by non-invasive imaging;

d) The non-invasive imaging is used to sense **a property within said region of a patient that is indicative of cell viability or inviability of transplanted progenitor or stem cells**; and

e) The **data from the sensing the property within said region is used to indicate cell viability from a transplant of progenitor or stem cells within the region**;

f) wherein said cell viability **is indicated by a property in cell chemistry resulting from an event** selected from the group consisting of cell activity, cell inactivity, cell growth, cell death, specific cell function, specific cell dysfunction, volumetric expansion of cell population, and volumetric decrease of cell population.

The Response to Argument section of the Examiner's answer never specifically addresses the performance of these recited steps. Instead, the "Response" states:

> "...various properties are **evaluated** [**emphasis added**] such as graft rejection, inflammation response, and tumor formation of the transplanted cells in a patient post-transplantation (col. 4 lines 7-15)."

The response then points to Example 4 as:

> "...clearly teaches conducting an MR evaluation in a patient post-transplantation checking for tumor growth and this would necessarily also mean checking for the viability of the transplanted cells since the cells were transplanted to inhibit tumor formation."

Looking at Example 4, reproduced below, it can be seen that all Major does in that example is to look and see if tumors are present, a direct image inspection, not a "...sensing of properties within a region resulting from an event..." as recited in the claims.

Major states in the cited text of Example 4:

> "EXAMPLE 4
> This example describes cerebral MRI evaluation one month following implantation of the four remaining monkeys. No evidence of tumor formation was present in any of the monkeys.
>
> "Following induction of anesthesia, **the monkeys were placed in a standard MRI frame. T_1 and T_2 weighted images without contrast and T_1 weighted images with gadolinium were done using a 1.5 Tesla magnet (Signa). The scans revealed no evidence of tumor or nodule formation (FIG. 9)**." (**emphasis** added)

That example shows nothing more than direct observation of a site to search for tumors.

The statement in the "Response" regarding the interpretation of Example 4 is in error, specifically on the issues of the present technology and the claims. For example, the "Response" states that "...the cells were transplanted to inhibit tumor formation." That is a total misunderstanding of the process and underlying science. Cells are implanted to form function-specific cells in the environment where they are implanted. If cells are implanted in the region of the pancreas, they are expected to form pancreatic cells. If they are implanted in the liver, they are expected to form liver cells, etc. At no time are cells implanted to replace or inhibit tumor cell formation. The problem actually addressed (as clearly stated in the specification) is that when cells are implanted, those implanted cells may themselves become or cause tumors, and the implanted cells may not remain viable in the patient.

Additionally, the attempted nexus between "checking for tumor growth" and "checking for the viability of the transplanted cells" completely ignores the fact that the MRI of Example 4 used to see if tumors are present cannot check for the viability of the transplanted cells. The transplanted cells would appear no different from cells already present in the environment. It is in fact, the indirect "...**sensing of properties within a region resulting from an event**..." (as opposed to attempting to merely forming an image the region) that enables detection of specifically cell viability. If significant numbers of the cells are viable, then the chemistry or chemical absorption properties (for example) in the region will change, and those changes can be **SENSED** as required by the claims. If significant numbers of cells become inviable (e.g., die), then different chemistry will occur in the region and that different chemistry can be **SENSED** as required by the claims. It is this indirect sensing of properties that is required in the practice of the invention, and it is this indirect sensing of properties that is not taught by Major and which step is erroneously avoided and circumvented in the new approach to the rejection of the claims.

This new approach is clearly in error and cannot be sustained.

Even more egregious in its approach is the assertion in the "Response" section that:

> "With respect to the quamtitative assessment of functionality, Major et al. teach MR evaluation and obtaining T1 and T2 weighted images with and without contrast and **therefore shows blood flow changes in the cells and necessarily provides a quantitative assessment of transplanted cells.**" (**emphasis** added)

Remeombering that the claims reciting quantitatively determining cell viability are active positive steps of using the sensed data to make a real determination of quantitative values, Major et al. do not even do what the Response states it does, has no disclosure of any blood flow changes in cells, and **ABSOLUTELY CANNOT AND DOES NOT PROVIDE A QUANTITATIVE ASSESSMENT OF CELL VIABILITY.**

First, the entire text of Major et al. has been searched and the only mention of "blood" in the entire text is the general definition that "As used herein, 'treating a host' includes prophylactic, palliative, and curative intervention in a disease process. The host may be any warm blooded mammal, such as humans, non-human primates, rodents, and the like."

The statement in the Response is clearly an assertion not based on the teachings of Major et al. The assertion attempts to make a legal conclusion of inherency without any basis for the statement or it underlying implications from the reference itself. There is absolutely no basis from the Major reference or any other reference of record in combination with Major et al. that even **SUGGESTS** sensing local properties and using data from the locally sensed properties to make a quantitative determination of cell viability. That step does not include direct imagery of a transplant site to view implanted cells. Direct imagery cannot make a quantitative determination of the small cell volumes implanted, as those transplanted cells are visually indistinguishable from native cells in the transplant region.

The response makes additional statements of inherency (e.g., "necessarily" is repeated on page 8 regarding "measuring various parameters."). Each of these references are merely erroneous, misinterpreting, and unwarranted legal conclusions that misconstrue the teachings of the reference and attempt to circumvent the need for an actual teaching of the recited limitations of the claims.

The secondary references (e.g., Marcos" cited to show "monitoring blood flow or changes in blood flow as vascular supply is developed) are not material to the sensing of a property, especially the recited chemical properties, and the use of the sensed data to determine cell viability. The Response again resorts to taking marginal technology and asserting materiality and obviousness in its combination with Major, when those combinations would not even produce the results required and recited in process steps in the claims.

These new approaches and issues to rejection of the claims are clear error in that they assume facts from the references that are not there (blood flow measurements in Major et al., which are non-existent, as necessarily providing quantitative measurements of cell viability) and then combine those non-existent facts into an assertion of an obvious process step.

These new approaches should not be sustained in the Appeal and all rejections should be reversed and all claims allowed.

ARGUMENT

Claims 5-7, 9, 11-26 and 29 have been rejected under 35 USC 103(a) as unpatentable over Lemelson (US Patent No. 5,865,744) in view of Palti (US Patent No. 5,190,041)

All previous arguments from the Brief on Appeal are retained and incorporated herein by reference.

All rejections have been traversed and overcome by these arguments.

CONCLUSION

All rejections of record have been shown in detail to be in error. The rejection should be reversed and all claims should be indicated as allowable.

Applicants believe the claims are in condition for allowance and request reconsideration of the application and allowance of the claims. The Examiner is invited to telephone the below-signed attorney at 952-832-9090 to discuss any questions that may remain with respect to the present application.

Respectfully submitted,
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Date 8 APRIL 2010 By _____
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I hereby certify that this correspondence is being sent by facsimile transmission or deposited with the United States Postal Service as first class mail in an envelope addressed to Box: APPEAL BRIEF - PATENTS, P.O. BOX 1450; Commissioner for Patents, Alexandria, VA 22313-1450 on 8 APRIL 2010.

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